AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-3. (cancelled)

4. (currently amended) A method for *in vitro* insertion of a nucleic acid of interest initially included in a DNA vector, within a predetermined target nucleotide sequence present in a chromosome contained in a target prokaryotic or eukaryotic cell that does not comprise said nucleic acid of interest at said target nucleotide sequence, said method comprising:

a) contacting ~~the~~ a DNA vector that is replication competent in said target prokaryotic or eukaryotic cell and comprises ~~comprising~~ the nucleic acid of interest~~, said DNA vector being replication competent in said prokaryotic or eukaryotic cell,~~ with a mutagenic agent blocking ~~the~~ intracellular DNA replication of said DNA vector ~~in the cell~~, to produce a modified DNA vector;

b) transfecting said target prokaryotic or eukaryotic cells with the modified DNA vector obtained at the end of step a) under conditions wherein replication of said modified DNA vector

commences and insertion of the nucleic acid of interest within said predetermined target nucleotide sequence occurs; and

c) selecting prokaryotic or eukaryotic cells for which the nucleic acid of interest has been integrated into the predetermined target nucleotide sequence as a result of said transfecting of step b).

5. (previously presented) The method according to claim 4, further comprising

selecting from the prokaryotic or eukaryotic cells obtained in step c), the cells wherein the DNA vector sequences, other than those of the nucleic acid of interest, were removed.

6. (previously presented) The method according to claim 4, wherein the mutagenic agent is selected from the group consisting of: N-acetoxy-2-acetylaminofluorene (N-AcO-AAF), an alkylating agent, benzo(a) pyrene-diol-epoxyde (BPDE) and UV irradiation.

7. (previously presented) The method according to claim 5, wherein the mutagenic agent is N-acetoxy-2-acetylaminofluorene (N-AcO-AAF).

8. (previously presented) The method according to claim 7, wherein in step a), the N-AcO-AAF is contacted with the DNA

vector comprising the nucleic acid of interest, at a concentration adapted for binding at least 10 N-AcO-AAF molecules per molecule of the polynucleotide.

9. (previously presented) The method according to claim 8, wherein the concentration of N-AcO-AAF is adapted for binding at least 50 N-AcO-AAF molecules per molecule of the polynucleotide.

10. (previously presented) The method according to claim 4, wherein the nucleic acid of interest to be inserted into the chromosome of the prokaryotic or eukaryotic cell, being initially included in said DNA vector comprises respectively at its 5' terminus and at its 3' terminus, sequences having at least 99.5% identity with the corresponding sequences located at the 5' terminus and 3' terminus of the target DNA contained in the chromosome.

11. (previously presented) The method according to claim 10, wherein the sequences respectively located at the 5' terminus and at 3' terminus of the nucleic acid of interest are identical respectively to the 5' terminus and 3' terminus of the target DNA contained in the chromosome.

12. (previously presented) The method according to claim 4, wherein the nucleic acid of interest included in said DNA vector comprises a selection marker nucleotide sequence.

13. (previously presented) The method according to claim 4, wherein the nucleic acid of interest comprises an open reading frame that encodes a protein of therapeutic interest.

14. (previously presented) The method according to claim 4, wherein the nucleic acid of interest comprises an open reading frame disrupted by a heterologous nucleotide sequence.

15. (previously presented) The method according to claim 4, wherein the nucleic acid of interest encodes an antisense RNA.

16. (previously presented) The method according to claim 13, wherein the nucleic acid of interest further comprises a nucleotide sequence with a promoter function, being functional in the selected prokaryotic or eukaryotic host cell, under the control of which the open reading frame or the sequence encoding the RNA included in said nucleic acid of interest is operably arranged.

17. (previously presented) The method according to claim 4, wherein the nucleic acid comprising the nucleic acid of interest comprises a marker nucleotide sequence located, in said polynucleotide, outside the nucleotide sequence of the nucleic acid of interest.

18. (previously presented) The method according to claim 4, wherein said DNA vector is a bacterial plasmid.

19. (previously presented) The method according to claim 4, wherein said DNA vector is a functional plasmid in bacterial cells.

20. (previously presented) The method according to claim 4, wherein said DNA vector is a functional plasmid in human cells.

21. (previously presented) The method according to claim 4, wherein the DNA vector is a double strand linear DNA.

22. (previously presented) The method according to claim 4, wherein the cells transfected in step b) comprise bacterial cells.

23. (previously presented) The method according to claim 4, wherein the cells transfected in step b) consist of non human mammalian cells.

24. (previously presented) The method according to claim 4, wherein the cells transfected in step b) consist of human cells.